Relationship between the kinetics of neuronal responses and the release of drugs from micropipettes: effect of retaining current

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A neurone can respond to the microelectrophoretic application of a drug by a change in its rate of firing. The time-course of this change is referred to as the kinetics of the neuronal response. It has been found that the time-course of the neuronal response is characteristic of the drug applied (Curtis & Crawford, 1969). As protagonists and antagonists can change the kinetics of a response evoked by an agonist, it is important to be able to evoke reproducible base-line responses. For this reason it is usual to apply ejecting current pulses of standard intensity and duration, but less importance is attributed to the parameters of the retaining current applied between drug ejections. We have examined the role of retaining currents in influencing the time-course of neuronal responses.

Excitatory responses of spontaneously active cortical neurones to microelectrophoretically applied glutamate, acetylcholine, noradrenaline, 5-hydroxytryptamine and mescaline were studied in the halothane anaesthetized cat. The response parameters measured were: latency of onset, maximum (equilibrium) firing rate, time taken to achieve the maximum firing rate, recovery time (after the termination of the ejecting current), total spike number (number of action potentials generated in response to the ejecting current pulse).

We have found that an increase in either parameter (intensity, duration of application) of the pre-ejection retaining current resulted in the prolongation of the response latency and of the time taken to achieve the maximum firing rate, but it did not alter the maximum firing rate itself. When ejecting current pulses of standard duration were used, an increase in either parameter of the retaining current reduced the magnitude (total spike number) of the response. An increase in the intensity of the post-ejection retaining current reduced the recovery time of the response.

We have attempted to relate these observations to changes in the rate of release of drugs from micropipettes by measuring the release of ^{14}C-noradrenaline *in vitro*. We have found that increases in either parameter of the retaining current reduced the amount of noradrenaline released during standard applications of an ejecting current.

Our results suggest that the gradual change in firing rate which takes place during a drug application in part reflects a gradual increase in the rate of release from the micropipette. A stable maximum or minimum firing rate cannot be achieved until the rate of release has reached an equilibrium value. It is concluded that standard neuronal responses can only be achieved if the standard ejecting current pulses give rise to identical pulses of drug release. To ensure this, it is necessary to keep both parameters of the retaining current constant. It is not meaningful to compare the time-courses of neuronal responses without specifying these parameters.

REFERENCE

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The effects of acetylsalicylic acid on the metabolic availability of ascorbic acid in man (T)

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